Survey of Health Care–Associated Infections

TO THE EDITOR: Magill et al. (March 27 issue)[1] report a 4% prevalence of health care–associated infections among 11,282 patients from 183 U.S. hospitals. In our view, an important limitation of the study is the ascertainment of patients. By exclusively including patients who were receiving antimicrobial agents, the authors may have missed a substantial proportion of patients with health care–associated infections, despite their assumption that the use of antimicrobial therapy is a highly sensitive indicator for these infections.[2] An established national prevalence surveillance system from the Netherlands reported that only 71.9% of the patients with a health care–associated infection received antimicrobial drugs at the moment of inclusion.[3] The extent of this underestimation probably depends on the type of infection and local treatment guidelines, but it may be as high as one third of all cases and will, moreover, lead to a flawed distribution of types of health care–associated infections and their causative microorganisms. Depending on the exact methods used, the distribution of types of health care–associated infections may furthermore be influenced by the fact that Magill and colleagues chose a cross-sectional approach (limiting the number of patients included per hospital).

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: We agree with Voss and Hopman that the use of antimicrobial treatment to identify patients with health care–associated infections is a potential limitation, as we acknowledged in the Supplementary Appendix (available with the full text of our article at NEJM.org). On the basis of data from our earlier surveys[1] we believe that this approach was justified in our survey of 183 U.S. hospitals, in which the use of antimicrobial agents was prevalent. However, this approach may not be justified in other countries. In the Dutch national surveys and in a European Centre for Disease Prevention and Control (ECDC) prevalence survey of health care–associated infections and the use of antimicrobial agents in 2011–2012,[2] antimicrobial treatment was more narrowly defined and less prevalent than in our survey. Although 39.9% of the patients in our survey met antimicrobial screening criteria that prompted review for health care–associated infections, just 23.3% of patients in Dutch hospitals in the ECDC survey would have met similar criteria on the basis of antimicrobial agents administered on the survey date.[2] ECDC data also showed that in hospitals outside the Netherlands, 95.5% of health care–associated infections, as compared with 81.3% of these infections in the Netherlands, occurred in patients who were receiving antimicrobial agents.[2] The Centers for Disease Control and Prevention recommends that all U.S. hospitals implement antimicrobial stewardship programs.[3] As prescribing of antimicrobial agents improves, it will be important to reassess the sensitivity of our screening approach.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the Agency for Toxic Substances and Disease Registry.

Since publication of their article, the authors report no further potential conflict of interest.

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2012. Stockholm: European Center for Disease Prevention and Control, 2013 (http://www.ecdc.europa.eu/en/publications/publications/healthcare-associated-infections-antimicrobial-use-pps.pdf).

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Hyperimmune Globulin to Prevent Congenital CMV Infection

TO THE EDITOR: Revello et al. (April 3 issue)[1] report the results of a randomized, placebo-controlled, phase 2 trial of hyperimmune globulin for the prevention of maternofetal cytomegalovirus (CMV) transmission. This study was based on the findings of a nonrandomized 2005 study by Nigro et al.[2] Both studies, as well as the retrospective observational study by Buxmann et al.,[3] used monthly administration of hyperimmune globulin, based on the assumption of a terminal elimination half-life of 22.4 days for total IgG antibodies.[4] We reassessed the pharmacokinetic characteristics of the CMV-specific antibody response[5] in a volunteer pregnant woman with proven CMV primary infection who received intravenous hyperimmune globulin every 4 weeks. We found periodic decreases in CMV-IgG levels with a half-life of about 11 days, along with fluctuations in epitope-specific recombinant CMV IgG avidity and repeated decreases in epithelial-cell–specific neutralization capacity. These findings may have an effect on clinical outcome. Therefore, we suggest a reanalysis of the pharmacokinetics of hyperimmune globulin–induced, compartment-specific CMV antibody and CMV neutralization capacity in plasma, amniotic fluid, and cord blood in order to redefine an optimized treatment schedule for the administration of hyperimmune globulin.

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2. Nigro G, Adler SP, La Torre R, Best AM. Passive immunization during pregnancy for congenital cytomegalovirus infection. N Engl J Med 2005;353:1350-62.
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TO THE EDITOR: Revello et al. report that the use of CMV-specific hyperimmune globulin did not significantly alter the course of congenital CMV infection in their study. However, several aspects of the study design could have led to an underestimation of the effect. First, hyperimmune globulin was discontinued when testing of amniotic fluid was positive for CMV. An observational study showed that in women with CMV-positive amniotic fluid, the use of hyperimmune globulin mitigated fetal infection.[1] It is unclear whether these pregnancies were terminated. Second, three women delivered a fetus with congenital CMV despite negative results on amniocentesis. Although an interval of 6 to 8 weeks between the presumed onset of maternal infection and amniocentesis is described for these three women, it is unknown whether the same interval after maternal infection was respected in all patients.[2] Third, the statistical power of the study by Revello et al. was based on an absolute reduction of 24 percentage points (a relative reduction of 60%) in clinical infections, as described previously.[1] Although the between-group difference was not significant, the observed absolute reduction in CMV infection among women receiving hyperimmune globulin was 14 percentage points. However, the 95% confidence interval was −3 to 31, which does not exclude a clinically relevant effect. A larger study is needed to draw definite conclusions.